ESO guideline for the management of extracranial and intracranial artery dissection

Supplementary Panel 1

Populations:

Extracranial artery dissection (EAD)
EAD patients with acute ischemic stroke
symptomatic EAD patients with acute ischemic stroke, transient ischemic attack (TIA), retinal ischemia, or local symptoms only, and without subarachnoid hemorrhage (SAH)
post-acute EAD patients with a stenosis or a dissecting aneurysm and no SAH
IAD
IAD patients with acute ischemic stroke
symptomatic IAD patients with acute ischemic stroke, TIA, retinal ischemia, or local symptoms only, and without SAH
post-acute IAD patients with a stenosis or a dissecting aneurysm and no SAH
IAD (intracranial dissecting aneurysm) with SAH
IAD with headache only

Interventions & Comparators:

Intervention	**Comparator**
targeting hyperacute phase recanalization (ischemic stroke by IAD or EAD)	
IV thrombolysis	no IV thrombolysis
endovascular treatment (mechanical thrombectomy or treatment of the dissection)	no endovascular treatment
targeting acute phase treatment or prevention of SAH	
endovascular or surgical treatment of IAD	optimal medical treatment alone
targeting prevention of recurrences, complications	
anticoagulant	antiplatelet
endovascular or surgical treatment	optimal medical treatment alone

Outcomes:

death
functional outcome (mRS 0-2 vs 3-6, 0-1 vs 2-6, or equivalent)
ischemic stroke
SAH
intracerebral hemorrhage (ICH)
major bleeding

Supplementary Material

Search Strategy

I: Targeting hyperacute phase recanalization (ischemic stroke by IAD or EAD)
PICO 1: In EAD & IAD patients with acute ischemic stroke is IV thrombolysis vs no IV thrombolysis associated with a reduced risk of death and of unfavorable functional outcome (mRS 0-2 vs 3-6, or 0-1 vs 2-6, or equivalent) and no increased risk of ICH, SAH, or other major bleeding*?

1. ((extracranial artery dissection) OR (vertebral artery dissection) OR (carotid artery dissection) OR (carotid artery, internal, dissection) OR (cervical artery dissection)).ti,ab,tw.
2. exp carotid artery injuries/
3. carotid artery, internal, dissection/
4. (carotid adj5 (injur$ or dissection or trauma$).tw.
5. (((carotid arteries) OR (carotid artery diseases) OR (carotid artery thrombosis)) AND ((aneurysm, dissecting) OR (aneurysm, ruptured) OR (wounds OR Injur* OR nonpenetrating) OR dissection)).ti,ab,tw.
6. (traumatic adj5 (dissection or aneurysm or pseudoaneurysm)).tw.
7. (blunt adj5 (injur$ or trauma)).tw.
8. dissecting aneurysm.tw.
9. ((intracranial OR intradural OR intracranial aneurysm OR (intracranial artery diseases)) AND dissection).ti,ab,tw.
10. ((internal carotid artery dissection) OR (carotid artery, internal, dissection) OR (middle cerebral artery fenestration) OR (middle cerebral artery fenest*) OR (middle cerebral artery dissection) OR (posterior inferior cerebellar artery dissection) OR (anterior inferior cerebellar artery dissection) OR (basilar artery dissection) OR (intracerebral artery dissection) OR (intracranial artery dissection)).ti,tw,ab.
11. (#1 to #10), OR
12. ((stroke) OR (CVA) OR (cerebrovascular accident*) OR (cerebrovascular infarct*) OR (cerebrovascular embolism) OR (brain ischemia) OR (brain infarct*) OR (brain haemorrhage) OR (brain infarction) OR (ischemic stroke) OR (cerebral embolism) OR (cerebral haemorrhage) OR (cardioembolic stroke) OR (thrombotic CVA) or (thrombotic infarct) OR (cerebrovascular disorder)).ti,tw,ab.
13. cerebrovascular disease/
14. cerebral artery disease/
15. cerebrovascular accident/
16. stroke/
17. vertebrobasilar insufficiency/
18. carotid artery disease/
19. exp carotid artery obstruction/
20. exp brain infarction/
21. exp brain ischemia/
22. exp occlusive cerebrovascular disease/
23. stroke patient/
24. (isch?emi$ adj6 (stroke$ or cerebral vasc$ or cerebrovasc$ or cva or attack$)).tw.
25. ((brain or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebr$ or mca$ or anterior circulation) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw.
26. (#12 to #25), OR

27. ((tPA) OR (plasminogen activator*) OR (tissue plasminogen activator*) OR (recombinant tissue plasminogen activator*) OR (rtPA) OR (rt-PA) OR (alteplase) OR (reteplase) OR (tenecteplase) OR (recombinant protein*) OR fibrinolytic* OR fibrinolytic agent* OR (fibrinolytic therapy) OR urokinase OR anistreplase OR streptokinase OR thrombolytic* OR plasmin OR (blood clot lysis)).ti,tw,ab.
28. fibrinolytic therapy/
29. fibrinolytic agent/
30. plasmin/
31. plasminogen/
32. exp plasminogen activator/
33. blood clot lysis/
34. fibrinolysis/
35. (thromboly$ or fibrinoly$ or recanalis$ or recanaliz$).tw.
36. ((clot$ or thrombus) adj5 (lyse or lysis or dissolve$ or dissolution)).tw.
37. (tPA or t-PA or rtPA or rt-PA or plasminogen or plasmin or alteplase or actilyse).tw.
38. (anistreplase or streptodornase or streptokinase or urokinase or pro?urokinase or rpro?uk or lumbrokinase or duteplase or lanoteplase or pamiteplase or reteplase or saruplase or staphylokinase or streptase or tenecteplase or desmoteplase or retevase).tw.
39. (#27 to #38), OR
40. #11 AND #26 AND #39
41. #40 AND (Humans* AND English)

PICO 2: In EAD & IAD patients with acute ischemic stroke is endovascular treatment (stenting and/or thrombectomy) vs no endovascular treatment (with or without IV thrombolysis) associated with a reduced risk of death and of unfavorable functional outcome (mRS 0-2 vs 3-6, or 0-1 vs 2-6, or equivalent) and no increased risk of ICH, SAH, or other major bleeding?

1. ((extracranial artery dissection) OR (vertebral artery dissection) OR (carotid artery dissection) OR (carotid artery, internal, dissection) OR (cervical artery dissection)).ti,ab,tw.
2. exp carotid artery injuries/
3. carotid artery, internal, dissection/
4. (carotid adj5 (injur$ or dissection or trauma$).tw.
5. (((carotid arteries) OR (carotid artery diseases) OR (carotid artery thrombosis)) AND ((aneurysm, dissecting) OR (aneurysm, ruptured) OR (wounds OR Injur* OR nonpenetrating) OR dissection)).ti,ab,tw.
6. (traumatic adj5 (dissection or aneurysm or pseudoaneurysm)).tw.
7. (blunt adj5 (injur$ or trauma)).tw.
8. dissecting aneurysm.tw.
9. ((intracranial OR intradural OR intracranial aneurysm OR (intracranial artery diseases)) AND dissection).ti,ab,tw.
10. ((internal carotid artery dissection) OR (carotid artery, internal, dissection) OR (middle cerebral artery fenestration) OR (middle cerebral artery fenest*) OR (middle cerebral artery dissection) OR (posterior inferior cerebellar artery dissection) OR (anterior inferior cerebellar artery dissection) OR (basilar artery dissection) OR (intracerebral artery dissection) OR (intracranial artery dissection)).ti,tw,ab.
11. (#1 to #10), OR
12. ((stroke) OR (CVA) OR (cerebrovascular accident*) OR (cerebrovascular infarct*) OR (cerebrovascular embolism) OR (brain ischemia) OR (brain infarct*) OR (brain haemorrhage) OR (brain infarction) OR (ischemic stroke) OR (cerebral embolism) OR (cerebral haemorrhage) OR (cardioembolic stroke) OR (thrombotic CVA) or (thrombotic infarct) OR (cerebrovascular disorder)).ti,tw,ab.
13. cerebrovascular disease/
14. cerebral artery disease/
15. cerebrovascular accident/
16. stroke/
17. vertebrobasilar insufficiency/
18. carotid artery disease/
19. exp carotid artery obstruction/
20. exp brain infarction/
21. exp brain ischemia/
22. exp occlusive cerebrovascular disease/
23. stroke patient/
24. (isch?emi$ adj6 (stroke$ or cerebral vasc$ or cerebrovasc$ or cva or attack$)).tw.
25. ((brain or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebr$ or mca$ or anterior circulation) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw.
26. (#12 to #35), OR
27. (thrombectomy OR endovascular OR trapping OR stent-retriever OR aspiration OR (tandem occlusion) OR surgical* OR neurosurgical OR coil* OR endovascular coiling OR flow-diverter* OR flow diverting stent* OR stent OR embolization OR pipeline embolization OR surgery OR surgical repair OR microsurgery OR microneurosurgery OR clip* OR clipping OR surgical clipping OR (neurosurgical clipping) OR (angioplasty) OR (angioplasty, balloon) OR (angioplasty, laser)).ti,tw,ab.

28. angioplasty/ or angioplasty, balloon/ or angioplasty, balloon, laser-assisted/ or angioplasty, laser/ Stents/
29. (angioplasty or stent$ or endovascular).ti,tw,ab.
30. balloon adj5 (dilat$ or catheter$).tw.
31. (endoluminal or transluminal) adj5 repair$.tw.
32. (#27 to #31), OR
33. (#11 AND #26 AND #32)
34. #33 AND (Human* AND English)

II Targeting acute phase treatment or prevention of SAH

PICO 3: In IAD patients with an intracranial dissecting aneurysm and a subarachnoid hemorrhage (SAH) does endovascular or surgical treatment of the aneurysm vs optimal medical treatment alone reduce the risk of SAH recurrence, ICH, death and of unfavorable functional outcome (mRS 0-2 vs 3-6, or 0-1 vs 2-6, or equivalent)?

1. ((intracranial OR intradural OR intracranial aneurysm OR (intracranial artery diseases)) AND dissection).ti,ab,tw.
2. ((internal carotid artery dissection) OR (carotid artery, internal, dissection) OR (middle cerebral artery fenestration) OR (middle cerebral artery fenest*) OR (middle cerebral artery dissection) OR (posterior inferior cerebellar artery dissection) OR (anterior inferior cerebellar artery dissection) OR (basilar artery dissection) OR (intracerebral artery dissection) OR (intracranial artery dissection)).ti,tw,ab.
3. #1 OR #2
4. Exp aneurysm*/ OR (aneurysm*).ti,ab,tw.
5. (cranial OR intracranial OR cerebral OR brain OR intracerebral).ti,ab,tw.
6. #4 AND #5
7. ((subarachnoid hemorrhage) OR (subarachnoid bleeding) OR (SAH)).ti,ab,tw.
8. #3 AND #6 AND #7
9. (thrombectomy OR endovascular OR trapping OR stent-retriever OR aspiration OR (tandem occlusion) OR surgical* OR neurosurgical OR coil* OR endovascular coiling OR flow-diverter* OR flow diverting stent* OR stent OR embolization OR pipeline embolization OR surgery OR surgical repair OR microsurgery OR microneurosurgery OR clip* OR clipping OR surgical clipping OR (neurosurgical clipping) OR (angioplasty) OR (angioplasty, balloon) OR (angioplasty, laser)).ti,tw,ab.
10. angioplasty/ or angioplasty, balloon/ or angioplasty, balloon, laser-assisted/ or angioplasty, laser/ Stents/
11. (angioplasty or stent$ or endovascular).ti,tw,ab.
12. balloon adj5 (dilat$ or catheter$).tw.
13. (endoluminal or transluminal) adj5 repair$.tw.
14. (#9 to #13), OR
15. #8 AND #14
16. #15 AND (Human* AND English)

PICO 4: In symptomatic IAD patients with an intracranial dissecting aneurysm and isolated headache (no TIA, no acute ischemic stroke, no SAH) does endovascular or surgical treatment of the aneurysm vs optimal medical treatment alone reduce the risk of ischemic stroke, SAH, ICH, death and of unfavorable functional outcome (mRS 0-2 vs 3-6, or 0-1 vs 2-6, or equivalent)?

1. ((intracranial OR intradural OR intracranial aneurysm OR (intracranial artery diseases)) AND dissection).ti,ab,tw.
2. ((internal carotid artery dissection) OR (carotid artery, internal, dissection) OR (middle cerebral artery fenestration) OR (middle cerebral artery fenest*) OR (middle cerebral artery dissection) OR (posterior inferior cerebellar artery dissection) OR (anterior inferior cerebellar artery dissection) OR (basilar artery dissection) OR (intracerebral artery dissection) OR (intracranial artery dissection)).ti,tw,ab.
3. #1 OR #2
4. Exp aneurysm*/ OR (aneurysm*).ti,ab,tw.
5. (cranial OR intracranial OR cerebral OR brain OR intracerebral).ti,ab,tw.
6. #4 AND #5
7. (Headache OR Cephalagia OR (Neck pain) OR Migraine OR (head pain) OR (pain, head) OR Tension headache).ti,ab,tw.
8. ((subarachnoid hemorrhage) OR (subarachnoid bleeding) OR (SAH)).ti,ab,tw.
9. (TIA OR acute ischemic stroke).ti,ab,tw.
10. #8 OR #9
11. #7 NOT #10
12. #3 AND #6 AND #11
13. (thrombectomy OR endovascular OR trapping OR stent-retriever OR aspiration OR (tandem occlusion) OR surgical* OR neurosurgical OR coil* OR endovascular coiling OR flow-diverter* OR flow diverting stent* OR stent OR embolization OR pipeline embolization OR surgery OR surgical repair OR microsurgery OR microneurosurgery OR clip* OR clipping OR surgical clipping OR (neurosurgical clipping) OR (angioplasty) OR (angioplasty, balloon) OR (angioplasty, laser)).ti,tw,ab.
14. angioplasty/ or angioplasty, balloon/ or angioplasty, balloon, laser-assisted/ or angioplasty, laser/ Stents/
15. (angioplasty or stent$ or endovascular).ti,tw,ab.
16. balloon adj5 (dilat$ or catheter$).tw.
17. (endoluminal or transluminal) adj5 repair$.tw.
18. (#13 to #17), OR
19. #12 AND #18
20. #19 AND (Human* AND English)

III Targeting prevention of recurrences, complications

PICO 5: In symptomatic EAD & IAD patients with ischemic stroke, TIA, retinal ischemia, or with local† symptoms only, and without SAH, is anticoagulant treatment at the acute phase of the dissection vs antiplatelet therapy associated with a reduced risk of ischemic stroke (occurrence or recurrence), death and of unfavorable functional outcome (mRS 0-2 vs 3-6, 0-1 vs 2-6, or equivalent) and with no increased risk of ICH, SAH, other major bleeding?**

1. ((extracranial artery dissection) OR (vertebral artery dissection) OR (carotid artery dissection) OR (carotid artery, internal, dissection) OR (cervical artery dissection)).ti,ab,tw.
2. exp carotid artery injuries/
3. carotid artery, internal, dissection/
4. (carotid adj5 (injur$ or dissection or trauma$).tw.
5. (((carotid arteries) OR (carotid artery diseases) OR (carotid artery thrombosis)) AND ((aneurysm, dissecting) OR (aneurysm, ruptured) OR (wounds OR Injur* OR nonpenetrating) OR dissection)).ti,ab,tw.
6. (traumatic adj5 (dissection or aneurysm or pseudoaneurysm)).tw.
7. (blunt adj5 (injur$ or trauma)).tw.
8. dissecting aneurysm.tw.
9. ((intracranial OR intradural OR intracranial aneurysm OR (intracranial artery diseases)) AND dissection).ti,ab,tw.
10. ((internal carotid artery dissection) OR (carotid artery, internal, dissection) OR (middle cerebral artery fenestration) OR (middle cerebral artery fenest*) OR (middle cerebral artery dissection) OR (posterior inferior cerebellar artery dissection) OR (anterior inferior cerebellar artery dissection) OR (basilar artery dissection) OR (intracerebral artery dissection) OR (intracranial artery dissection)).ti,tw,ab.
11. (#1 to #10), OR
12. ((stroke) OR (CVA) OR (cerebrovascular accident*) OR (cerebrovascular infarct*) OR (cerebrovascular embolism) OR (brain ischemia) OR (brain infarct*) OR (brain haemorrhage) OR (brain infarction) OR (ischemic stroke) OR (cerebral embolism) OR (cerebral haemorrhage) OR (cardioembolic stroke) OR (thrombotic CVA) or (thrombotic infarct) OR (cerebrovascular disorder)).ti,tw,ab.
13. cerebrovascular disease/
14. cerebral artery disease/
15. cerebrovascular accident/
16. stroke/
17. vertebrobasilar insufficiency/
18. carotid artery disease/
19. exp carotid artery obstruction/
20. exp brain infarction/
21. exp brain ischemia/
22. exp occlusive cerebrovascular disease/
23. stroke patient/
24. (isch?emi$ adj6 (stroke$ or cerebral vasc$ or cerebrovasc$ or cva or attack$)).tw.
25. ((brain or cerebr$ or cerebell$ or vertebrobasil$ or hemispher$ or intracran$ or intracerebral or infratentorial or supratentorial or middle cerebr$ or mca$ or anterior circulation) adj5 (isch?emi$ or infarct$ or thrombo$ or emboli$ or occlus$ or hypoxi$)).tw.
26. (TIA or transient ischemic stroke OR ((minor OR mini OR mild OR warning) AND stroke) OR (transient brain ischemia) OR Retinal ischemia OR (Retinal artery occlusion)).ti,tw,ab.
27. (#12 to #26), OR
28. ((aspirin) OR (antiplatelet*) OR (dual antiplatelet therap*) OR (DAPT) OR (anticoagula*) OR (thienopyridine Derivatives) OR (clopidogrel) OR (ticlopidine) OR (dipyridamole) OR (prasugrel)

OR (terutroban) OR (sarpogrelate) OR (cilostazol) OR (triflusal) OR (platelet aggregation inhibitor) OR (acetylsalicylic acid) OR (indobufen)).ti,tw,ab.

29. exp platelet aggregation inhibitors/
30. P2Y12 inhibitors/
31. gp2b3a inhibitors
32. blood platelets/
33. platelet aggregation/
34. (antiplatelet$ or antithromb$ or anticoag$).tw.
35. (aspirin or acetylsalicylic acid or indobufen).tw.
36. (dipyridamole or ticlopidine or clopidogrel or sulfinpyrazone or sulphinpyrazone).tw.
37. (heparin$ or coumarin$ or coumadin$ or warfarin).tw.
38. ((Anticoagulant) OR (vitamin K antagonist*) OR (VKA) OR (warfarin) OR (phenprocoumon) OR (acenocoumarol) OR (fluindione) OR (tecarfarin) OR (novel oral anticoagulant) OR (direct oral anticoagulants) OR (oral anticoagulants) OR (DOAC) or (oral anticoagulants) OR (non-vitamin K antagonist oral anticoagulants) OR (NOAC*) OR (novel anticoagulants) OR (Pradaxa) OR (apixaban) OR (Dabigatran) OR (edoxaban) OR (rivaroxaban) OR (Xa inhibitors) OR (Ximelagatran) OR (Xa inhibitor)).ti,tw,ab.
39. exp anticoagulants/
40. (#28 to #39), OR
41. #11 AND #27 AND #40
42. #40 AND (Human* AND English)

PICO 6: In EAD patients and in non-SAH IAD patients does endovascular or surgical treatment of a stenosis or a dissecting aneurysm outside the acute phase vs optimal medical treatment alone reduce the risk of death, ischemic stroke, ICH, and SAH?

1. ((extracranial artery dissection) OR (vertebral artery dissection) OR (carotid artery dissection) OR (carotid artery, internal, dissection) OR (cervical artery dissection)).ti,ab,tw.
2. exp carotid artery injuries/
3. carotid artery, internal, dissection/
4. (carotid adj5 (injur$ or dissection or trauma$).tw.
5. (((carotid arteries) OR (carotid artery diseases) OR (carotid artery thrombosis)) AND ((aneurysm, dissecting) OR (aneurysm, ruptured) OR (wounds OR Injur* OR nonpenetrating) OR dissection)).ti,ab,tw.
6. (traumatic adj5 (dissection or aneurysm or pseudoaneurysm)).tw.
7. (blunt adj5 (injur$ or trauma)).tw.
8. dissecting aneurysm.tw.
9. (#1 TO #8), OR
10. ((intracranial OR intradural OR intracranial aneurysm OR (intracranial artery diseases)) AND dissection).ti,ab,tw.
11. ((internal carotid artery dissection) OR (carotid artery, internal, dissection) OR (middle cerebral artery fenestration) OR (middle cerebral artery fenest*) OR (middle cerebral artery dissection) OR (posterior inferior cerebellar artery dissection) OR (anterior inferior cerebellar artery dissection) OR (basilar artery dissection) OR (intracerebral artery dissection) OR (intracranial artery dissection)).ti,tw,ab.
12. (#10 OR #11)
13. ((subarachnoid hemorrhage) OR (subarachnoid bleeding) OR (SAH)).ti,ab,tw.
14. #12 NOT #13
15. (#9 OR #14)
16. (thrombectomy OR endovascular OR trapping OR stent-retriever OR aspiration OR (tandem occlusion) OR surgical* OR neurosurgical OR coil* OR endovascular coiling OR flow-diverter* OR flow diverting stent* OR stent OR embolization OR pipeline embolization OR surgery OR surgical repair OR microsurgery OR microneurosurgery OR clip* OR clipping OR surgical clipping OR (neurosurgical clipping) OR (angioplasty) OR (angioplasty, balloon) OR (angioplasty, laser)).ti,tw,ab.
17. angioplasty/ or angioplasty, balloon/ or angioplasty, balloon, laser-assisted/ or angioplasty, laser/ Stents/
18. (angioplasty or stent$ or endovascular).ti,tw,ab.
19. balloon adj5 (dilat$ or catheter$).tw.
20. (endoluminal or transluminal) adj5 repair$.tw.
21. (#16 to #20), OR
22. (#15 AND #21)
23. #22 AND (Human* AND English)

Supplementary Table 1.1: Risk of bias assessment of observational comparative studies using the SIGN 50 checklist for PICO1

	Internal validity														Overall
Author	**Conduct of study**	**Selection of subjects**					**Assessment**						**Confounders**	**Analysis**	**ROB***
	1.1	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**1.11**	**1.12**	**1.13**	**1.14**	**2.1**
Bernardo 2019	Yes	No	NA	Yes	NR	No	Yes	No	CS	Yes	CS	NA	Yes	Yes	+
Dziewas 2003	Yes	No	NA	Yes	NR	No	Yes	No	CS	Yes	Yes	NA	Yes	No	+
Engelter 2012	Yes	No	Yes	Yes	Yes	No	Yes	No	CS	Yes	Yes	NA	Yes	Yes	+
Qureshi 2011	Yes	No	NA	Yes	NR	No	Yes	No	CS	Yes	Yes	NA	Yes	Yes	+

1.1: The study addresses an appropriate and clearly focused question; 1.2: The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation; 1.3: The study indicates how many of the people asked to take part did so, in each of the groups being studied; 1.4. The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis; 1.5: What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed; 1.6: Comparison is made between full participants and those lost to follow up, by exposure status; 1.7: The outcomes are clearly defined; 1.8: The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable; 1.9: Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome; 1.10: The method of assessment of exposure is reliable; 1.11: Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable; 1.12: Exposure level or prognostic factor is assessed more than once; 1.13: The main potential confounders are identified and taken into account in the design and analysis; 1.14: Have confidence intervals/p value been provided? 2.1: How well was the study done to minimise the risk of bias or confounding?
CS: Can't say, NA: Not applicable; NR: Not reported; *Reading guide: guide: **High quality** (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+): Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies

Supplementary Table 1.2: Risk of bias assessment of observational comparative studies using the SIGN 50 checklist for PICO2

	Internal validity														Overall
Author	**Conduct of study**	**Selection of subjects**					**Assessment**						**Confounders**	**Analysis**	**ROB***
	1.1	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**1.11**	**1.12**	**1.13**	**1.14**	**2.1**
Bernardo 2019	Yes	No	NA	Yes	NR	No	Yes	No	CS	Yes	CS	NA	Yes	Yes	+
Jensen 2017	Yes	No	NA	Yes	NR	No	Yes	No	CS	Yes	Yes	NA	Yes	Yes	+
Li 2018	Yes	Yes	NA	Yes	NR	No	Yes	No	CS	Yes	Yes	NA	Yes	No	+
Marnat 2020	Yes	No	NA	Yes	NR	No	Yes	No	CS	Yes	Yes	NA	Yes	Yes	+
Traenka 2018	Yes	No	Yes	Yes	Yes	NA	Yes	No	CS	Yes	Yes	NA	Yes	Yes	+

1.1: The study addresses an appropriate and clearly focused question; 1.2: The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation; 1.3: The study indicates how many of the people asked to take part did so, in each of the groups being studied; 1.4. The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis; 1.5: What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed; 1.6: Comparison is made between full participants and those lost to follow up, by exposure status; 1.7: The outcomes are clearly defined; 1.8: The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable; 1.9: Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome; 1.10: The method of assessment of exposure is reliable; 1.11: Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable; 1.12: Exposure level or prognostic factor is assessed more than once; 1.13: The main potential confounders are identified and taken into account in the design and analysis; 1.14: Have confidence intervals/p value been provided? 2.1: How well was the study done to minimise the risk of bias or confounding?

CS: Can't say, NA: Not applicable; NR: Not reported; *Reading guide: guide: **High quality** (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+): Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies

Supplementary Table 1.3: Risk of bias assessment of observational comparative studies using the SIGN 50 checklist for PICO3

	Internal validity														Overall
Author	**Conduct of study**	**Selection of subjects**					**Assessment**						**Confounding**	**Analysis**	**ROB***
	1.1	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**1.11**	**1.12**	**1.13**	**1.14**	**2.1**
Anxionnat 2003	Yes	Yes	No	Yes	NA	NA	Yes	No	CS	Yes	CS	NA	NA†	NA†	+
Mizutani 1995	Yes	CS	NA	Yes	NA	NA	Yes	No	CS	Yes	CS	NA	NA†	NA†	+
Rabinov 2003	Yes	CS	No	Yes	Yes	No	Yes	No	CS	Yes	CS	NA	NA†	NA†	+
Zhao 2007	Yes	CS	No	Yes	Yes	No	Yes	No	CS	Yes	CS	NA	NA†	NA†	+

1.1: The study addresses an appropriate and clearly focused question; 1.2: The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation; 1.3: The study indicates how many of the people asked to take part did so, in each of the groups being studied; 1.4. The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis; 1.5: What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed; 1.6: Comparison is made between full participants and those lost to follow up, by exposure status; 1.7: The outcomes are clearly defined; 1.8: The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable; 1.9: Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome; 1.10: The method of assessment of exposure is reliable; 1.11: Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable; 1.12: Exposure level or prognostic factor is assessed more than once; 1.13: The main potential confounders are identified and taken into account in the design and analysis; 1.14: Have confidence intervals/p value been provided? 2.1: How well was the study done to minimise the risk of bias or confounding?

CS: Can't say, NA: Not applicable; *Reading guide: guide: **High quality** (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+): Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies; † these studies are descriptive and do not provide association statistics

Supplementary Table 1.4: Risk of bias assessment of observational comparative studies using the SIGN 50 checklist for PICO4

Not applicable

Supplementary Table 1.5: Risk of bias assessment of observational comparative studies using the SIGN 50 checklist for PICO5

	Internal validity														Overall
Author	**Conduct of study**	**Selection of subjects**					**Assessment**						**Confounders**	**Analysis**	**ROB ***
	1.1	**1.2**	**1.3**	**1.4**	**1.5**	**1.6**	**1.7**	**1.8**	**1.9**	**1.10**	**1.11**	**1.12**	**1.13**	**1.14**	**2.1**
Arnold 2006	Yes	CS	No	NA	Yes	No	Yes	No	CS	Yes	Yes	NA	Yes	Yes	+
Arauz 2006	Yes	CS	No	NA	Yes	NA	Yes	No	CS	Yes	CS	NA	Yes	Yes	+
Ast 1993	Yes	CS	CS	CS	CS	CS	CS	CS	CS	CS	CS	CS	CS	No†	CS
Beletsky 2003	Yes	CS	No	Yes	Yes	No	Yes	No	CS	Yes	CS	NA	No	No	+
Caprio 2014	Yes	No	CS	NA	Yes	Yes	Yes	No	CS	Yes	No	NA	No	No	+
Daou 2017	Yes	No	CS	NA	Yes	No	Yes	No	CS	Yes	No	NA	Yes	Yes	+
Dziewas 2003	Yes	No	CS	NA	Yes	NA	Yes	No	CS	Yes	No	NA	Yes	No†	+
Gensicke 2015	Yes	CS	No	NA	Yes	NA	Yes	No	CS	Yes	Yes	NA	Yes‡	Yes	+
Georgiadis 2009	Yes	No	No	NA	Yes	NA	Yes	No	CS	Yes	No	NA	Yes	Yes	+
Kennedy 2012	Yes	No	No	Yes	Yes	No	Yes	No	CS	Yes	No	NA	No	No	+
Metso 2009	Yes	CS	No	Yes	Yes	No	Yes	No	CS	Yes	No	NA	CS	No†	+
Ramchand 2018	Yes	CS	No	Yes	Yes	NA	Yes	No	CS	Yes	Yes	NA	Yes	Yes	+

1.1: The study addresses an appropriate and clearly focused question; 1.2: The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation; 1.3: The study indicates how many of the people asked to take part did so, in each of the groups being studied; 1.4. The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis; 1.5: What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed; 1.6: Comparison is made between full participants and those lost to follow up, by exposure status; 1.7: The outcomes are clearly defined; 1.8: The assessment of outcome is made blind to exposure status. If the study is retrospective this may not be applicable; 1.9: Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome; 1.10: The method of assessment of exposure is reliable; 1.11: Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable; 1.12: Exposure level or prognostic factor is assessed more than once; 1.13: The main potential confounders are identified and taken into account in the design and analysis; 1.14: Have confidence intervals/p value been provided? 2.1: How well was the study done to minimise the risk of bias or confounding?
CS: Can't say, NA: Not applicable; *Reading guide: guide: **High quality** (++): Majority of criteria met. Little or no risk of bias. Results unlikely to be changed by further research. **Acceptable** (+): Most criteria met. Some flaws in the study with an associated risk of bias, Conclusions may change in the light of further studies. **Low quality** (0): Either most criteria not met, or significant flaws relating to key aspects of study design. Conclusions likely to change in the light of further studies; † raw figures and OR(95%CI) obtained from previously published meta-analyses;[1,2] ‡ only for stroke severity analyses due to small sample size

Supplementary Table 1.6: Risk of bias assessment of observational comparative studies using the SIGN 50 checklist for PICO6

Not applicable

Supplementary Table 7: Eligible articles considered for the qualitative synthesis of all the PICOs

	Randomized clinical trials	Observational studies
PICO1	-	Bernardo et al, Int J Stroke 2019[3] Dziewas et al, J Neurol 2003[4] Engelter et al, Eur J Neurol 2012[5] Qureshi et al, Arch Neurol 2011[6]
PICO2	-	Bernardo et al, Int J Stroke 2019[3] Jensen et al, J Neurointerv Surg 2017[7] Li et al, Stroke 2018[8] Marnat et al, Stroke 2020[9] Traenka et al, Eur Stroke J 2018[10]
PICO3	-	Anxionnat et al, Neurosurgery 2003[11] Mizutani et al, Neurosurgery 1995[12] Rabinov et al, Am J Neuroradiol 2003[13] Zhao et al, Acta Neurochir (Wien) 2007[14]
PICO4	-	Ahn et al, Am J Neuroradiol 2006[15] Naito et al, Neurosurgery 2002[16] Nakazawa et al, Neuroradiol J 2011[17] Nam et al, J Neurointerv Surg 2015[18] Kobayashi et al, Am J Neuroradiol 2014[19]
PICO5	Markus et al, Lancet Neurol 2015[20] Markus et al, JAMA Neurol 2019[21] Engelter et al, Lancet Neurol 2021[22]	Arauz et al, Cerebrovasc Dis 2006[23] Arauz et al, Eur J Neurol 2013[24] Ast et al, Eur J Med 1993[25] Beletsky et al, Stroke 2003[26] Caprio et al, Cerebrovasc Dis 2014[27] Daou et al, Neurosurgery 2017[28] Dziewas et al, J Neurol 2003[4] Gensicke et al, Eur J Neurol 2015[29] Georgiadis et al, Neurology 2009[30] Kennedy et al, Neurology 2012[31] Metso et al, Eur J Neurol 2009[32] Ramchand et al, J Stroke Cerebrovasc Dis 2018[33]
PICO6	-	Moon et al, J Neurointerv Surg 2017[34] Müller et al, J Vasc Surg 2000[35]

REFERENCES

1. Lyrer P, Engelter S. Antithrombotic drugs for carotid artery dissection. Cochrane Database Syst Rev 2010:CD000255.
2. Chowdhury MM, Sabbagh CN, Jackson D, Coughlin PA, Ghosh J. Antithrombotic treatment for acute extracranial carotid artery dissections: a meta-analysis. Eur J Vasc Endovasc Surg 2015;50:148-156.
3. Bernardo F, Nannoni S, Strambo D, et al. Efficacy and safety of endovascular treatment in acute ischemic stroke due to cervical artery dissection: A 15-year consecutive case series. Int J Stroke 2019;14:381-389.
4. Dziewas R, Konrad C, Dräger B, et al. Cervical artery dissection--clinical features, risk factors, therapy and outcome in 126 patients. J Neurol 2003;250:1179-1184.
5. Engelter ST, Dallongeville J, Kloss M, et al. Thrombolysis in cervical artery dissection--data from the Cervical Artery Dissection and Ischaemic Stroke Patients (CADISP) database. Eur J Neurol 2012;19:1199-1206.
6. Qureshi AI, Chaudhry SA, Hassan AE, et al. Thrombolytic treatment of patients with acute ischemic stroke related to underlying arterial dissection in the United States. Arch Neurol 2011;68:1536-1542.
7. Jensen J, Salottolo K, Frei D, et al. Comprehensive analysis of intra-arterial treatment for acute ischemic stroke due to cervical artery dissection. J Neurointerv Surg 2017;9:654-658.
8. Li S, Zi W, Chen J, et al. Feasibility of Thrombectomy in Treating Acute Ischemic Stroke Because of Cervical Artery Dissection. Stroke 2018;49:3075-3077.
9. Marnat G, Lapergue B, Sibon I, et al. Safety and Outcome of Carotid Dissection Stenting During the Treatment of Tandem Occlusions: A Pooled Analysis of TITAN and ETIS. Stroke 2020;51:3713-3718.
10. Traenka C, Jung S, Gralla J, et al. Endovascular therapy versus intravenous thrombolysis in cervical artery dissection ischemic stroke - Results from the SWISS registry. Eur Stroke J 2018;3:47-56.
11. Anxionnat R, de Melo Neto JF, Bracard S, et al. Treatment of hemorrhagic intracranial dissections. Neurosurgery 2003;53:289-300; discussion 300-281.
12. Mizutani T, Aruga T, Kirino T, Miki Y, Saito I, Tsuchida T. Recurrent subarachnoid hemorrhage from untreated ruptured vertebrobasilar dissecting aneurysms. Neurosurgery 1995;36:905-911; discussion 912-903.
13. Rabinov JD, Hellinger FR, Morris PP, Ogilvy CS, Putman CM. Endovascular management of vertebrobasilar dissecting aneurysms. AJNR Am J Neuroradiol 2003;24:1421-1428.
14. Zhao WY, Krings T, Alvarez H, Ozanne A, Holmin S, Lasjaunias P. Management of spontaneous haemorrhagic intracranial vertebrobasilar dissection: review of 21 consecutive cases. Acta Neurochir (Wien) 2007;149:585-596; discussion 596.
15. Ahn JY, Han IB, Kim TG, et al. Endovascular treatment of intracranial vertebral artery dissections with stent placement or stent-assisted coiling. AJNR Am J Neuroradiol 2006;27:1514-1520.
16. Naito I, Iwai T, Sasaki T. Management of intracranial vertebral artery dissections initially presenting without subarachnoid hemorrhage. Neurosurgery 2002;51:930-937; discussion 937-938.
17. Nakazawa T, Takeichi Y, Yokoi T, et al. Treatment of spontaneous intradural vertebral artery dissections. Neuroradiol J 2011;24:699-711.
18. Nam KH, Ko JK, Cha SH, Choi CH, Lee TH, Lee JI. Endovascular treatment of acute intracranial vertebral artery dissection: long-term follow-up results of internal trapping and reconstructive treatment using coils and stents. J Neurointerv Surg 2015;7:829-834.
19. Kobayashi N, Murayama Y, Yuki I, et al. Natural course of dissecting vertebrobasilar artery aneurysms without stroke. AJNR Am J Neuroradiol 2014;35:1371-1375.

20. Markus HS, Hayter E, Levi C, Feldman A, Venables G, Norris J. Antiplatelet treatment compared with anticoagulation treatment for cervical artery dissection (CADISS): a randomised trial. Lancet Neurol 2015;14:361-367.
21. Markus HS, Levi C, King A, Madigan J, Norris J. Antiplatelet Therapy vs Anticoagulation Therapy in Cervical Artery Dissection: The Cervical Artery Dissection in Stroke Study (CADISS) Randomized Clinical Trial Final Results. JAMA Neurol 2019;76:657-664.
22. Engelter ST, Traenka C, Gensicke H, et al. Aspirin versus anticoagulation in cervical artery dissection (TREAT-CAD): an open-label, randomised, non-inferiority trial. Lancet Neurol 2021;20:341-350.
23. Arauz A, Hoyos L, Espinoza C, Cantú C, Barinagarrementeria F, Román G. Dissection of cervical arteries: Long-term follow-up study of 130 consecutive cases. Cerebrovasc Dis 2006;22:150-154.
24. Arauz A, Ruiz A, Pacheco G, et al. Aspirin versus anticoagulation in intra- and extracranial vertebral artery dissection. Eur J Neurol 2013;20:167-172.
25. Ast G, Woimant F, Georges B, Laurian C, Haguenau M. Spontaneous dissection of the internal carotid artery in 68 patients. Eur J Med 1993;2:466-472.
26. Beletsky V, Nadareishvili Z, Lynch J, Shuaib A, Woolfenden A, Norris JW. Cervical arterial dissection: time for a therapeutic trial? Stroke 2003;34:2856-2860.
27. Caprio FZ, Bernstein RA, Alberts MJ, et al. Efficacy and safety of novel oral anticoagulants in patients with cervical artery dissections. Cerebrovasc Dis 2014;38:247-253.
28. Daou B, Hammer C, Mouchtouris N, et al. Anticoagulation vs Antiplatelet Treatment in Patients with Carotid and Vertebral Artery Dissection: A Study of 370 Patients and Literature Review. Neurosurgery 2017;80:368-379.
29. Gensicke H, Ahlhelm F, Jung S, et al. New ischaemic brain lesions in cervical artery dissection stratified to antiplatelets or anticoagulants. Eur J Neurol 2015;22:859-865, e861.
30. Georgiadis D, Arnold M, von Buedingen HC, et al. Aspirin vs anticoagulation in carotid artery dissection: a study of 298 patients. Neurology 2009;72:1810-1815.
31. Kennedy F, Lanfranconi S, Hicks C, et al. Antiplatelets vs anticoagulation for dissection: CADISS nonrandomized arm and meta-analysis. Neurology 2012;79:686-689.
32. Metso TM, Metso AJ, Salonen O, et al. Adult cervicocerebral artery dissection: a single-center study of 301 Finnish patients. Eur J Neurol 2009;16:656-661.
33. Ramchand P, Mullen MT, Bress A, et al. Recanalization after Extracranial Dissection: Effect of Antiplatelet Compared with Anticoagulant Therapy. J Stroke Cerebrovasc Dis 2018;27:438-444.
34. Moon K, Albuquerque FC, Cole T, Gross BA, McDougall CG. Stroke prevention by endovascular treatment of carotid and vertebral artery dissections. J Neurointerv Surg 2017;9:952-957.
35. Müller BT, Luther B, Hort W, Neumann-Haefelin T, Aulich A, Sandmann W. Surgical treatment of 50 carotid dissections: indications and results. J Vasc Surg 2000;31:980-988.